DRAFT
Risk Assessment Approach for Evaluating Potential Risks from Consuming Breast Milk

One of the remaining questions we have for the Portland Harbor human health risk assessment is how to evaluate potential risks to infants from consuming chemicals in breast milk as a result of maternal exposure from eating contaminated fish. EPA and its partners evaluated the feasibility of conducting a risk assessment based on exposure to breast milk using EPA's *Human Health Risk Assessment Protocol for Hazard Waste Combustion Facilities* (EPA 530-R-05-006, September 2005), and examples from other hazardous waste sites, such as the Housatonic river project in Massachusetts (*Human Health Risk Assessment, GE/Housatonic River Site, Rest of River*, Volume 1, EPA, February 2005). We determined that it is feasible to include exposure to breast milk in the Portland Harbor inwater risk assessment, and that this is an important exposure pathway.

To assist the Lower Willamette Group in incorporating the breast milk consumption pathway into the human health risk assessment, we prepared this memorandum to present the relevant exposure and risk equations, and exposure and toxicity parameters (summarized in Table 1). We include example calculations using total PCBs to show how the various equations in EPA's combustion guidance can be modified to focus on the fish consumption pathway. The actual risk assessment should include all relevant chemicals, such as PCB congeners, chlorinated dibenzo-*p*-dioxins, chlorinated dibenzofurans, and DDT and its degradation products.

Calculated Exposure to Infants

We mainly use the equations presented in the EPA combustion risk assessment guidance document, modified to make the equations no longer specific to dioxins or the inhalation pathway, and instead make them appropriate for fish consumption. The key concept is that the concentration of a chemical in milk can be calculated from the long-term body burden in the mother. We start with the average daily intake of chemicals from fish consumption (modified from Table C-1-4):

$$ADD_{mother} = \frac{C_{fish} \text{ x } IR_{fish} \text{ x } CF \text{ x } F_{fish}}{BW_{af}}$$

Where:

ADD_{mother}	=	Average daily dose to mother (mg/kg/day)
C_{fish}	=	Chemical concentration in fish (assume 1 mg/kg)
IR_{fish}	=	Ingestion rate of fish (subsistence rate of 142.4 g/day)
CF	=	Conversion factor (0.001 kg/g)
F_{fish}	=	Fraction of fish contaminated (1)
BW_{af}	=	Body weight (66 kg for average adult female)

The ingestion rate used in the example is for fishers subsisting on resident fish. The site risk assessment should include all of the relevant fish consumption rates. The fish consumption rate is an annualized rate (*i.e.*, it includes the assumption that fish are eaten throughout the year, so exposure frequency, exposure duration, and averaging time are not included in the equation). Loss of chemicals during cooking has been considered at other sites, but is not included in EPA's guidance. For body weight, we consider it appropriate to use the average female weight of 66 kg, rather than the guidance value of 70 kg (average adult weight).

For this example, the calculations are performed assuming a total PCB concentration of 1 mg/kg in fish tissue. Although this is close to the mean PCB concentration measured in Portland Harbor resident fish, the value was primarily chosen here for convenience. The actual risk assessment should use chemical concentrations appropriate for the various species of fish sampled.

$$ADD_{mother} = 1 \text{ mg/kg} \times 142.4 \text{ g/day} \times 0.001 \text{ kg/g} \times 1 / 66 \text{ kg} = 0.0022 \text{ mg/kg/day}$$

EPA has found that dietary intake of PCBs during pregnancy and lactation is only weakly correlated with PCB concentrations in human milk. The more important determinant is long-term consumption. The following equation (modified from Table C-3-1) is used to calculate the PCB concentration in milk fat. This assumes that maternal long-term intake occurs over a period greater than the PCB half-life, and that PCB concentrations in breast milk reflect the maternal body burden.

$$C_{milkfat} = \frac{ADD_{mother} \times h \times f_1}{\ln(2) \times f_2}$$

Where:

$C_{milkfat}$	= PCB concentration in milkfat (mg/kg-lipid)
ADD_{mother}	= Average daily dose to mother (mg/kg/day)
h	= Half-life of PCB (7 years = 2555 days)
f_1	= Fraction of ingested PCB stored in fat (0.9)
f_2	= Fraction of mother's weight that is fat (0.3 kg-lipidBW/kg-totalBW)

$$C_{milkfat} = \frac{0.0022 \text{ mg/kg-totalBW/day} \times 2555 \text{ days} \times 0.9}{0.693 \times 0.3 \text{ (kg-lipidBW/kg-totalBW)}}$$

$$= 24 \text{ mg/kg-lipid}$$

For the derivation of this equation, see Attachment A.

Average daily doses to the infant are calculated separately for carcinogenic and noncarcinogenic effects. For carcinogenic effects, the average daily dose is the following (modified from Table C-3-2):

$$ADD_{ca\text{-}child} = \frac{C_{milkfat} \times IR_{milk} \times f_3 \times f_4 \times ED_c \times EF_c}{AT_c \times BW_c}$$

Where:

$ADD_{ca\text{-}child}$	= Average daily dose for breast-feeding child (mg/kg/day)
$C_{milkfat}$	= Concentration of chemical in milk fat (mg/kg-lipid)
IR_{milk}	= Ingestion rate of breast milk (0.69 kg/day)
f_3	= Fraction of breast milk that is fat (0.04)
f_4	= Fraction of ingested PCB that is absorbed (0.9)
ED_c	= Exposure duration of breast-feeding child (1 year)
EF_c	= Exposure frequency of breast-feeding child (365 days/year)

AT_c	=	Averaging time – carcinogen (70 years x 365 days/year)
BW_c	=	Body weight of breast-feeding child (9.4 kg)

$$ADD_{ca\text{-}child} = \frac{24 \text{ mg/kg-lipid} \times 0.69 \text{ kg/day} \times 0.04 \times 0.9 \times 1 \text{ yr} \times 365 \text{ day/yr}}{70 \text{ yr} \times 365 \text{ day/yr} \times 9.4 \text{ kg}}$$

$$= 0.00091 \text{ mg/kg/day}$$

For non-cancer effects, the average daily dose is the following (modified from Table C-3-2):

$$ADD_{nc\text{-}child} = \frac{C_{milkfat} \times IR_{milk} \times f_3 \times f_4 \times ED_c \times EF_c}{AT_c \times BW_c}$$

Where:

$ADD_{nc\text{-}child}$	=	Average daily dose for breast-feeding child (mg/kg/day)
$C_{milkfat}$	=	Concentration of chemical in milk fat (mg/kg-lipid)
IR_{milk}	=	Ingestion rate of breast milk (0.69 kg-milk/day)
f_3	=	Fraction of breast milk that is fat (0.04 kg-lipid/kg-milk)
f_4	=	Fraction of ingested PCB that is absorbed (0.9)
ED_c	=	Exposure duration of breast-feeding child (1 year)
EF_c	=	Exposure frequency of breast-feeding child (365 days/year)
AT_{nc}	=	Averaging time – non-carcinogen (= ED_c x EF_c)
BW_c	=	Body weight of breast-feeding child (9.4 kg)

$$ADD_{nc\text{-}child} = \frac{24 \text{ mg/kg-lipid} \times 0.69 \text{ kg-milk/day} \times 0.04 \text{ kg-lipid/kg-milk} \times 0.9 \times 1 \text{ yr} \times 365 \text{ day/yr}}{1 \text{ yr} \times 365 \text{ day/yr} \times 9.4 \text{ kg}}$$

$$= 0.063 \text{ mg/kg/day}$$

Calculated Risk to Infants

Using the standard risk characterization equations, excess lifetime cancer risk and non-cancer hazards are calculated separately. Excess lifetime cancer risk is approximated by:

$$ELCR_{child} = ADD_{child} \times SF_o$$

Where:

$ELCR_{child}$	=	Excess lifetime cancer risk to child from breast feeding
SF_o	=	Cancer slope factor – oral [2 $(\text{mg/kg/day})^{-1}$ for total PCBs]

$$ELCR_{child} = 0.00091 \text{ mg/kg/day} \times 2 \ (\text{mg/kg/day})^{-1} = 2 \times 10^{-3}$$

The non-cancer hazard quotient is:

$$HQ_{child} = \frac{ADD_{child}}{RfD}$$

Where:
HQ_{child} = Hazard quotient for breast-feeding child
RfD = Non-cancer reference dose (2×10^{-5} mg/kg/day for total PCBs)

$$HQ_{child} = 0.063 \text{ mg/kg/day} / 2 \times 10^{-5} \text{ mg/kg/day} = 3{,}200$$

Using this approach, the excess lifetime cancer risk for a child consuming total PCBs in breast milk for one year is approximately 2×10^{-3}. This is unacceptable compared with an acceptable risk level of 1×10^{-6}. For non-cancer effects, the hazard quotient is 3,200, which is unacceptable compared with an acceptable hazard quotient of 1.

The calculated risks are based on an assumed total PCB concentration in resident fish of 1 mg/kg. Although this concentration was used mostly as a convenient value to demonstrate the calculations, it is approximately the concentration of total PCBs in resident fish in the initial study area of the lower Willamette River. Because the calculated excess lifetime cancer risk and hazard quotient are considerably above acceptable levels, we conclude that infant exposure to chemicals in breast milk is an important pathway for the Portland Harbor human health risk assessment.

Uncertainty Evaluation

Following standard guidance, the risk assessment for this pathway should include an evaluation of the associated uncertainties. During EPA's evaluation of this pathway, we considered the following.

The only exposure to infants evaluated was consumption of breast milk. We did not consider other potential exposure routes, such as transplacental transfer of PCBs from mother to fetus during pregnancy.

The PCB RfD is based on LOAELs developed from studies on monkeys. The health effects included inflammation of glands in the eye, distorted growth of finger and toe nails, and decreased antibody responses. The uncertainty factors used in the derivation of the human health RfD total 300, applied to an animal LOAEL of 0.005 mg/kg/day. The calculated HQ from consumption of breast milk is an order of magnitude greater than the uncertainty factor.

Another uncertainty is the application of the RfD to one year of exposure, rather than long-term (lifetime) exposure. EPA considers it appropriate to apply the RfD in this case, considering the potential sensitivity of infants to adverse health effects.

We also looked at the reduction in body burden of PCB during a year of breast feeding to see if that could result in substantially reduced concentrations in breast milk. If the concentration in milk fat (C_{milk} = 24 mg/kg-lipid) is equivalent to the concentration in other tissues (C_{lipid}), then the body burden in the mother is:

$C_{lipid} \times BW_{af} \times f_2 =$

24 mg/kg-lipid x 66 kg-BW x 0.3 kg-lipid/kg-BW = 480 mg PCB

The loss of mass during one year of breast feeding is:

$IR_{milk} \times C_{milkfat} \times f_3 \times 365$ days =

0.69 kg/day x 24 mg/kg-lipid x 0.04 kg-lipid/kg-milk x 365 days = 240 mg PCB

This implies that a mother will lose approximately half of her PCB body burden (240 mg / 480 mg) during a year of breast feeding, assuming that there is no additional consumption of contaminated fish during this period. This simplistic evaluation is consistent with EPA's determination (summarized in the GE/Housatonic report) that there will be a 20 percent reduction of PCBs in the mother every three months. Over a year, this would correspond to a reduction of $1 - (0.8)^4 = 0.6$, or a 60 percent reduction in PCB mass after one year. The reduction in mass (and concentration) averaged over the course of the year would be about half of this value. Refining the calculations to include this reduction in mass would alter the conclusions by a factor of about 2.

At other sites, including the Housatonic River site, EPA presented the potential risks from breast milk consumption as a ratio to background risk rather than as an excess lifetime cancer risk or hazard quotient. The background total PCB concentration that they use is 0.32 mg/kg-lipid in milk. Using the assumed total PCB concentration of 1 mg/kg in fish tissue and the assumed subsistence fish consumption rate, the calculated total PCB concentration in breast milk is 24 mg/kg-lipid. As an alternative presentation of risk in the uncertainty section, this result can be discussed as corresponding to a risk 75 times that of background concentrations.

EPA is aware that in the lower Willamette River, consumption of resident fish by lactating mothers is already discouraged by the PCB fish advisory. The Oregon Department of Human Services advisory states that:

> Women of childbearing age, particularly pregnant or breastfeeding women, children and people with weak immune systems, thyroid or liver problems, should avoid eating resident fish from Portland Harbor, especially carp, bass and catfish.

For this reason, there may currently be limited infant exposure to breast milk contaminated as a result of consumption of resident fish in the lower Willamette River. However, the results presented here appear to quantitatively support the advisory, and indicate that there are potentially unacceptable risks by this pathway.

Table 1
Parameters for Evaluation of Risk from Consuming Breast Milk

Parameter	Units	Description	Value
ADD_{mother}	mg/kg/day	Average daily dose to mother	Calculated
$ADD_{ca\text{-}child}$	mg/kg/day	Average daily dose to child (cancer)	Calculated
$ADD_{nc\text{-}child}$	mg/kg/day	Average daily dose to child (non-cancer)	Calculated
C_{fish}	mg/kg	Chemical concentration in fish	Calculated from site data. Assume 1 for example.
IR_{fish}	g/day	Ingestion rate of fish	142.4 for subsistence fishers
IR_{milk}	kg/day	Ingestion rate of breast milk	0.69
CF	kg/g	Conversion factor	0.001
F_{fish}	unitless	Fraction of fish contaminated	1
BW_{af}	kg	Body weight of adult female	66
BW_c	Kg	Body weight of infant child	9.4
$C_{milkfat}$	mg/kg-lipid	Concentration in milkfat	Calculated
h	days	Half-life of chemical	2555 (7 years) for PCBs
f_1	unitless	Fraction of ingested chemical stored in fat	0.9 for PCBs
f_2	unitless	Fraction of mother's weight that is fat	0.3
f_3	unitless	Fraction of breast milk that is fat	0.04
f_4	unitless	Fraction of ingested chemicals that is absorbed	0.9 for PCBs
ED_c	year	Exposure duration of breast-feeding child	1
EF_c	days/year	Exposure frequency of breast-feeding child	365 days/year
AT_c	days	Averaging time – carcinogen	25550 (70 years)
AT_{nc}	days	Averaging time – non-carcinogen	= ED x EF
$ELCR_{child}$	risk	Excess lifetime cancer risk	Calculated
HQ_{child}	hazard	Hazard quotient	Calculated
SF_o	$(mg/kg/day)^{-1}$	Cancer slope factor – oral	2 for PCBs
RfD	(mg/kg/day)	Reference dose	2×10^{-5} for PCBs

Attachment A
Derivation of Equation for Chemical Concentrations in Milkfat

The EPA guidance documents do not elaborate on the derivation of the equation for calculation of chemicals present in milkfat. The main reference for the equation is *Infant Exposure Assessment for Breast Milk Dioxins and Furans Derived from Waste Incineration Emissions* (Allan H. Smith, Risk Analysis, Vol. 7, No. 3, 1987). In this attachment, we explicitly derive the equation used to approximate chemical concentrations in maternal body fat, which is assumed to be equivalent to the concentration in breast milk.

The chemical body burden in the mother is calculated assuming first-order kinetics:

$$B_t = B_0 \, e^{-kt}$$

Where:
t = time period (years)
B_t = Body burden at time t (mg)
B_0 = Body burden at time t = 0 (mg)
k = rate constant = ln(2) / h (days^{-1})
h = Half life of chemical in body (days)

Using a similar approach, the maternal daily chemical intake, m (mg/kg/day), is used to calculate the concentration of chemical in the mother's tissue. The contribution to maternal chemical levels (C_{mother} in mg/kg-body-weight) is:

$$C_{mother} = \int_0^T me^{-kt}\,dt$$

where the mother is exposed to chemicals in fish from time t = 0 to time t = T (in days). The general solution to this equation is:

$$\int_0^T me^{-kt}\,dt = \frac{me^{-kT}}{-k} - \frac{me^{0}}{-k} = \frac{me^{-[\ln(2)/h]T}}{-k} - \frac{m}{-k} = \frac{me^{-[\ln(2)][T/h]}}{-k} + \frac{m}{k}$$

$$= \frac{m\,(0.5)^{T/h}}{-k} + \frac{m}{k} = \frac{m}{k}\,[1 - (0.5)^{T/h}]$$

Substituting again for k = ln(2) / h,

$$C_{mother} = \frac{mh}{\ln(2)}\,[1 - (0.5)^{T/h}]$$

If the exposure period of the mother to contaminated fish (T) is equal to the chemical half-life (h) of 7 years for PCBs, then the chemical concentration in the mother's tissue is:

$$C_{mother} = 0.5\frac{mh}{\ln(2)}$$

If the exposure period of the mother to contaminated fish is equal to four half-lives (T = 4h = 28 years), then the chemical concentration in the mother's tissue is:

$$C_{mother} = 0.94\frac{mh}{\ln(2)}$$

The limit of $[1 - (0.5)^{T/h}]$ for large values of T (relative to the half-life h) is 1. Therefore, at exposure periods to the mother longer than the chemical half-life, a reasonably conservative assumption is that the chemical concentration in the mother can be approximated by:

$$C_{mother} = \frac{mh}{\ln(2)}$$

This equation is further refined by considering the fraction of the chemical stored in fat tissue (f_1) and the fraction of the mother's weight that is fat (f_2).

$$C_{mother} = \frac{mh}{\ln(2)}\frac{f_1}{f_2}$$

Substituting the symbol ADD_{mother} for m, and assuming that the chemical concentration in milkfat is equivalent to the chemical concentration in the mother's lipid tissue, yields the equation for $C_{milkfat}$ shown in the main text.

$$C_{milkfat} = \frac{ADD_{mother}\ h}{\ln(2)}\frac{f_1}{f_2}$$